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10/578,912	05/09/2006	Keiichirou Kai	1034232-000038	4449

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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 10/578,912
Filing Date: May 09, 2006
Appellant(s): KAI ET AL.

Roy Roberts
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed May 18, 2010 appealing from the Office action mailed November 25, 2009.

(1) Real Party in Interest

The examiner has no comment on the statement, or lack of statement, identifying by name the real party in interest in the brief.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The following is a list of claims that are rejected and pending in the application: 1, 4, and 6.

(4) Status of Amendments After Final

The examiner has no comment on the appellant's statement of the status of amendments after final rejection contained in the brief.

(5) Summary of Claimed Subject Matter

The examiner has no comment on the summary of claimed subject matter contained in the brief.

(6) Grounds of Rejection to be Reviewed on Appeal

The examiner has no comment on the appellant's statement of the grounds of rejection to be reviewed on appeal. Every ground of rejection set forth in the Office action from which the appeal is taken (as modified by any advisory actions) is being maintained by the examiner except for the grounds of rejection (if any) listed under the

subheading "WITHDRAWN REJECTIONS." New grounds of rejection (if any) are provided under the subheading "NEW GROUNDS OF REJECTION."

(7) Claims Appendix

The examiner has no comment on the copy of the appealed claims contained in the Appendix to the appellant's brief.

(8) Evidence Relied Upon

Tanaka, N. "Phosphorylation and dephosphorylation of polyhydroxy compounds by class A bacterial acid phosphatases" Org. Biomol. Chem., 2003, 1, 2833-2839.

Asano, Y. "A new enzymatic method of selective phosphorylation of nucleosides" Journal of Molecular Catalysis B: Enzymatic 6 (1999) 271-277.

Gross, A. "Practical Synthesis of 5-Phospho-D-ribosyl alpha-1-Pyrophosphate (PRPP): Enzymatic Routes from Ribose 5-Phosphate or Ribose" J. Am. Chem. Soc. 1983, 105, 7428-7435.

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 4, and 6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tanaka et al. (Org. Biomol. Chem., 2003, 1, 2833-2839, July 9, 2003, of record) in view of Asano et al. (Journal of Molecular Catalysis B: Enzymatic 6 (1999) 271-277, PTO-1449 submitted December 8, 2008), and Gross et al. (J. Am. Chem. Soc. 1983, 105, 7428-7435, of record). The following rejection was set forth in the office action mailed November 25, 2009 and is restated below.

Tanaka et al. teach the phosphorylation of inosine to inosine-5'-monophosphate by nonspecific acid phosphatases from *Shigella flexneri* [page 2834, second paragraph]. The enzyme also mediates the phosphorylation of glucose to glucose-6-phosphate using pyrophosphate as the phosphate donor [page 2835, last paragraph]. The specific activity of acid phosphatase derived from *Sh. flexneri* was 40 U mg^{-1} [page 2834, first paragraph]. In the enzymatic phosphorylation of inosine, 40mM inosine, 100mM disodium pyrophosphate, and 0.1-1μM of enzyme solution in a total volume of 1 ml was used [page 2838, last paragraph]. The amount of 5'-IMP increased with increasing PPi concentration [page 2834, Figure 2]. For the glucose phosphorylation, the reaction mixture contained 1μM PhoN, 100mM glucose and 100mM disodium pyrophosphate in 100mM sodium acetate [page 2839, first paragraph]. The classical chemical introduction of a phosphate group into a polyhydroxy compound is tedious, and since such structurally different compounds as glucose and inosine are able to enter the active site of the enzyme and were successfully phosphporylated, this method has potential as an alternative to chemical methods [page 2837, paragraph bridging the first and second column].

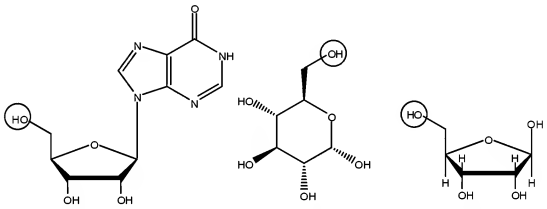
Tanaka et al. do not teach the phosphorylation of a free pentose and teach a 2.5:1 ratio of phosphate donor:pentose, not 3:1 to 7:1.

Asano teaches the enzymatic phosphorylation of inosine at the 5'-position. Reactions were carried out using 20 mg of inosine and 100 mg of tetrasodium pyrophosphate decahydrate [page 274, Table 1]. Considering that inosine has a molecular weight of about 268 and tetrasodium pyrophosphate decahydrate has a molecular weight of about 265, that corresponds to a molar ratio of about 376:75, or about 5:1.

Gross et al. teach that ribose 5-phosphate is an intermediate in the synthesis of nucleotides, histadine and tryptophan [page 7428, first paragraph]. Methods for preparing ribose 5-phosphate include obtaining the compound include chemical synthesis and enzyme-catalyzed synthesis using ribokinase [page 7429, Ribose 5-Phosphate].

It would have been obvious to one of ordinary skill in the art at the time the invention was made to prepare a pentose-5-phosphate ester using acid phosphatase from *Shigella flexneri* in the presence of pyrophosphate. Tanaka teaches the selective phosphorylation of inosine (a nucleoside derived from a pentose) and glucose (a hexose). Tanaka teaches a donor:pentose ratio of about 2.5:1, but also teaches that higher concentrations of phosphate donor lead to higher yields of the product. Asana teaches donor:pentose ratio of about 5:1 for screening enzymes for enzymatic phosphorylation of nucleosides, so the skilled artisan would be led to choose a similar ratio. The skilled artisan would expect the corresponding reaction to proceed on a

pentose in a substantially same or similar fashion because the structure of a pentose such as ribose is very similar to the structures of inosine and glucose with respect to the reaction sites, seen circled below. Further, Tanaka et al. teach that the enzyme is non-specific, and speculate that because it was effective for phosphorylation of inosine and glucose, that it might be widely applicable. The skilled artisan would have been motivated to prepare a pentose-5-phosphate ester because such compounds are useful intermediates in nucleotide synthesis, as taught by Gross et al., and are synthesized via chemical methods which Tanaka et al. teach can be replaced by methods utilizing acid phosphatase.



(10) Response to Argument

Appellant argues that the record contains evidence that the substrate specificity of the claimed enzyme cannot be predicted. Appellant arguments with respect to Tanaka's teachings are noted. However, Tanaka's p. 2835, first column, second paragraph refers to dephosphorylation, which is the reverse of the claimed phosphorylation (see Scheme 1). Tanaka's page 2834, first column, last paragraph

refers to the regioselectivity of phosphorylation, not substrate specificity. Tanaka teaches that Pho-N-Sf catalyzes the phosphorylation of inosine to inosine-5'-monophosphate (5'IMP), not inosine-3'-monophosphate (3'IMP). This means that the phosphorylation occurs at the position circled above, not the 3'-position (which is the OH nearest to the nucleoside base). Appellant argues that these structures are very similar, but they differ in that the 5' position is a primary hydroxyl, while the 3' position is a secondary hydroxyl. This is a significant difference. In all the structures shown above, the primary hydroxyl is the circled reacting site.

Appellant argues that Tanaka teaches that enzyme mechanisms are complex, and that Tanaka does not suggest that pentose could serve as a substrate for the enzyme. This argument is not persuasive because Tanaka teaches that the enzymatic method may be a useful alternative to existing chemical methods and that NSAP's have a wide range in substrate specificity [page 2638, first column, third paragraph].

Appellant argues that Appellant's data shows that the enzyme works on some pentoses and hexoses but not on others, which demonstrates the unpredictability of the field of art. This argument is noted, but is not persuasive because the skilled artisan has sufficient guidance to expect a successful reaction at least with ribose, based on Tanaka's teachings. Furthermore, Appellant's data shows that the reaction is successful on the majority of pentoses which were tried.

Appellant argues that Asano used intact cells of *Morganell morganii*, not the claimed acid phosphatase derived from *Shigella flexneri*. This argument is not persuasive because Asano teaches that *M. morganii* has phosphatase activity [page

275, second column]. Furthermore, Asano used the same ratio of inosine:phosphoric acid donor for screening many different microorganisms for phosphorotransferase activity (see page 274, Table 1), so the skilled artisan would expect that Asano's ratio would be effective and a reasonable starting point for an enymatic phosphorylation reaction.

Appellant argues that Gross teaches chemical methods for preparing ribose 5-phosphate, and Gross does not teach phosphorylation of a pentose by an acid phosphatase. This argument is not persuasive because Tanaka teaches that the enzymatic method could be used to replace chemical methods, and is widely applicable.

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

/Layla Bland/
Examiner, Art Unit 1623

Conferees:
/Shaojia Anna Jiang/
Supervisory Patent Examiner, Art Unit 1623

/Leigh C. Maier/
Primary Examiner, Art Unit 1623